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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,954	07/12/2001	M. Patricia Beckmann	2814-G	4147

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IMMUNEX CORPORATION
LAW DEPARTMENT
51 UNIVERSITY STREET
SEATTLE, WA 98101

EXAMINER
MERTZ, PREMA MARIA

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/904,954	Beckmann et al.
Examiner	**Art Unit**
Prema Mertz	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 25, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 3, 5, 7-15, and 28-39* is/are pending in the application.

4a) Of the above, claim(s) *28-39* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3, 5, and 7-15* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I (claims 1, 3, 5, 7-15) in Paper No. 6 (/9/25/02) is acknowledged. The traversal is on the ground(s) that examination of Groups I-III would cause no undue search requirement. This is not found persuasive because the searches for the 3 Groups would not overlap. Firstly, since Group I is directed to a nucleic acid of SEQ ID NO:1 or 3 (class 435, 69.1), Group II is drawn to a method of binding hek with a hek-L polypeptide (class 435, 7.1) and Group III is drawn to a method of binding elk with a hek-L polypeptide (class 435, 7.1), the searches for the 3 Groups would not overlap because the different inventions are classified in different classes and subclasses.

The test for propriety of restriction is not whether the inventions are related but rather whether they are distinct and whether it would impose a burden on the examiner to search and examine multiple inventions in a single invention. Group I and Groups II-III as related as a different product and different methods which are independent and distinct, each from the other, which possess characteristic differences in function and each has an independent utility, that is distinct for each invention which cannot be exchanged. The product of invention I is not used in the methods of inventions II-III.

Lastly the inventions are distinct because a search of the literature for the nucleic acid of Group I, would not be expected to reveal art for the methods of Groups II-III, which searches are extensive requiring separate searches which would be unduly burdensome. The nucleic acid of

Group I is not used in a method of binding hek of Group II nor is it used in a method of binding elk of Group III.

Having shown that these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different and recognized divergent subject matter as defined by MPEP.. § 808.02, the Examiner has *prima facie* shown a serious burden of search (see MPEP.. § 803). Therefore, an initial requirement of restriction for examination purposes as indicated is proper.

The Groups as delineated in the restriction requirement (Paper No. 4, 2/22/02) are patentably distinct one from the other such that each invention could, by itself, in principle, support its own separate patent (as shown by the arguments put forth in the written restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

Claims 28-30 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is suggested that the claims be amended to recite "DNA encoding a hek-ligand polypeptide".

Claim rejections-35 USC § 112, first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claims 1, 3, 5, 7-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim 1, 3, 5, 7 are genus claims and recite at least 80% identical", which encompasses nucleic acid variants of the DNA encoding hek-L protein. The term variant means a nucleic acid molecule encoding a protein having one or more amino acid substitutions, deletions, insertions and/or additions made to the DNA molecule which encodes the amino acid sequence set forth in claims 1, 3, 5, 7 (see page 8, lines 1-7). The specification and claims do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the nucleic acid molecule. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claims do not provide any guidance as to what changes should be made.

Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a nucleic acid encoding a protein set forth in claims, 1, 3, 5, 7 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicants were not in possession of the claimed genus of nucleic acid molecules.

3b. Claims 1, 3, 5, 7-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA encoding a hek-L protein, said DNA comprising a nucleotide sequence set forth in SEQ ID NO:1 or 3, does not reasonably provide enablement for an isolated DNA encoding a hek-L protein, said DNA comprising a nucleotide sequence that is at least 80% identical to a sequence set forth in SEQ ID NO:1 or 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 3, 5, 7, are overly broad, since no guidance is provided as to which of the myriad of nucleic acid molecules encoding polypeptide species encompassed by the claims will retain the characteristics of a hek-L polypeptide. Variants of the nucleic acid molecule encoding the hek-L polypeptide can be generated by conservative or nonconservative changes, allelic, splice species or

polymorphic variants (see pages 8-9). However, Applicants have failed to disclose any actual or prophetic examples on expected performance parameters of any of the possible nucleic acid molecules encoding muteins of hek-L polypeptide. Moreover, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding a hek-L polypeptide other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support

a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 1, 3, 5, 7, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 8-14 are rejected under 35 U.S.C. 112, first paragraph, insofar as they depend on claims 1, 3, 5, 7 for their limitations.

Claim rejections-Double Patenting

Non-statutory double patenting rejection (obviousness-type)

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA

1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4a. Claims 1, 5, 7-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 7-24 of U.S. Patent No. 5,516,658. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1-3, 19, 22 of U.S. Patent No. 5,516,658 (having all common inventors with the instant application), claims DNA that is encompassed within the scope of the claims of the DNA as recited in claims 1, 5, 7, of the instant application because the instant application recites a DNA that is at least 80% identical to the recited DNA fragments of SEQ ID NO:1. However, the patent claims are obvious from the instant claims because the patent claims are directed to one specific embodiment encompassed by the instant claims. The patented product is included in instant claims 1, 5, 7. It would have been obvious to one of ordinary skill in the art at the time the present invention was made, to perform sequential deletions of amino acids from the N-terminus or the C-terminus of the protein encoded by the claimed DNA of SEQ ID NO:1, to determine which amino acids are involved in the ligand binding to the

receptor or to make single amino acid substitutions to determine which amino acids in the ligand are important for ligand function. Since claims 1, 5, 7, recite "at least 80% identical" even a single amino acid change is encompassed by instant claims 1, 5, 7. The patented claims if infringed upon would also result in infringement of the broad claim of the instant application. Allowance of the pending claim, therefore, would have the effect of extending the enforceable life of the allowed claims beyond the statutory limit.

4b. Claims 3, 7-15 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-6, 7-24 of U.S. Patent No. 5,516,658. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 4-7, 19, 22 of U.S. Patent No. 5,516,658 (having all common inventors with the instant application), claims DNA that is encompassed within the scope of the claims of the DNA as recited, in claims 3, 7 of the instant application because the instant application recites a DNA that is at least 80% identical to the recited DNA fragments of SEQ ID NO:3. However, the patent claims are obvious from the instant claims because the patent claims are directed to one specific embodiment encompassed by the instant claims. The patented product is included in the instant claims. It would have been obvious to one of ordinary skill in the art at the time the present invention was made, to perform sequential deletions of amino acids from the N-terminus or the C-terminus of the protein encoded by the claimed DNA of SEQ ID NO:3, to determine which amino acids are involved in the ligand binding to the receptor or to make single amino acid substitutions to determine which amino acids in the ligand are important for ligand function. Since claims 3, 7, recite "at least 80% identical", even a single amino acid change

is encompassed by the instant claims 3, 7. The patented claims if infringed upon would also result in infringement of the broad claim of the instant application. Allowance of the pending claim, therefore, would have the effect of extending the enforceable life of the allowed claims beyond the statutory limit.

Conclusion

The claims are free of the prior art of record.

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
November 1, 2002